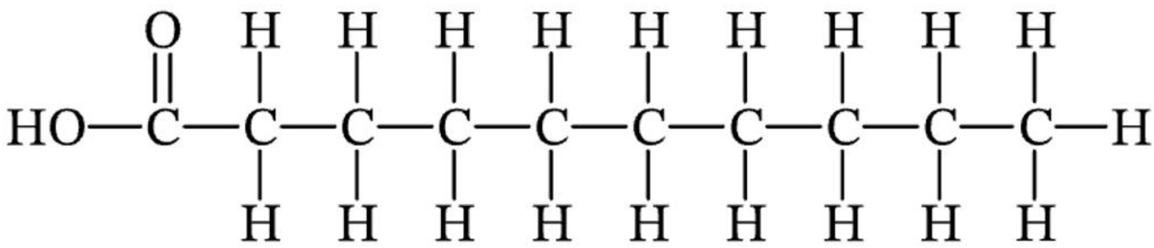
Exercise 1:
Atoms, bonds and non-covalent interactions

Question 1:

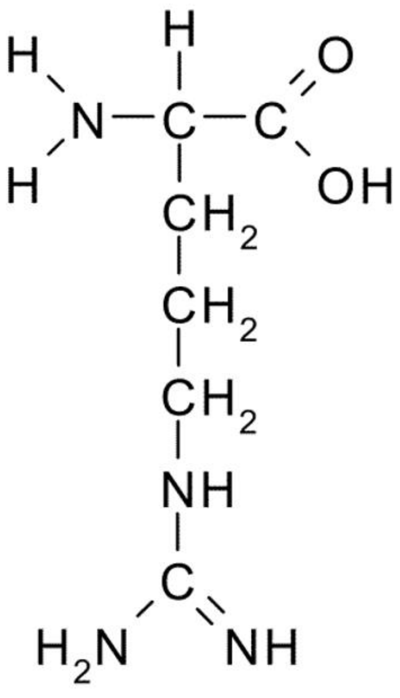
Below are some examples of biomolecule building blocks.

A



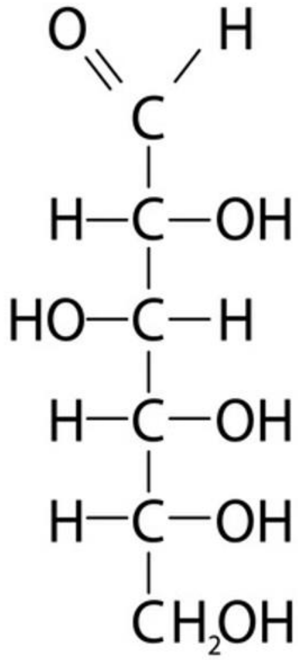
Capric acid

B



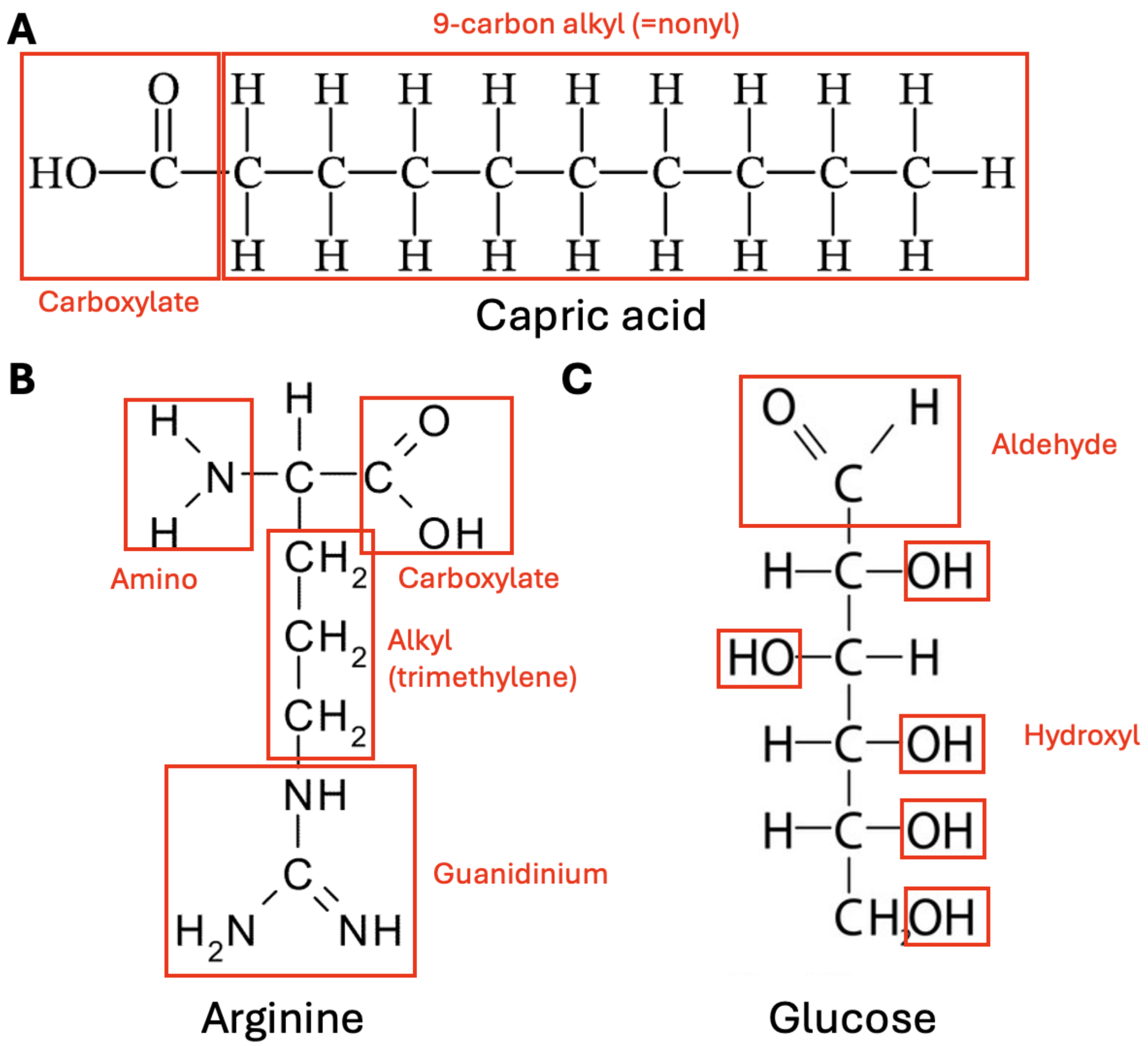
Arginine

C



Glucose

a) Can you identify and name different chemical groups in them?



b) Can you differentiate polar vs non-polar bonds?

All C-C and C-H bonds are non-polar.

Any C=O, C-O, C=N, C-N, O-H, N-H are polar.

c) Assuming aqueous solution at pH 7, what groups would be suitable for electrostatic interactions?

A: The carboxylate group would have negative charge (explained in the lecture)

B: Amino group would have positive charge. Carboxylate group would have negative charge. Guanidinium group can also bind a proton under these conditions and become positively charged.

C: None

d) What about hydrogen bonds?

All H atoms directly bound to O or N (but not C) can serve as hydrogen bond donors.

All O or N atoms can serve as hydrogen bond acceptors using their free electron pairs.

e) What about vdW interactions?

All atoms can engage in vdW depending on the local environment and their own polarizability.

f) Which of these molecules has the highest capacity to be hydrophobic?

Capric acid (A) has a long alkyl chain which is non-polar and therefore has high capacity to engage in hydrophobic effect (interactions). These molecules are called fatty acids and they are the building blocks of lipids, where hydrophobic effect plays a major role in their assembly and resulting functions.

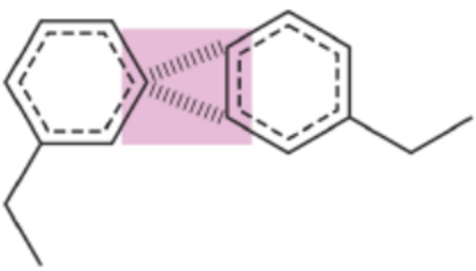
Question 2:

Here we classify bonds in four categories based on their dissociation energy (the change in energy when atoms are moved away from each other).

Strong: >200 kJ/mol
Medium: 20-200 kJ/mol
Weak: 5-20 kJ/mol
Very weak: 0-5 kJ/mol

Below four bond types are shown in purple.
(a) Name each bond-type and classify them into the four categories given above (in vacuum).
(b) Consider what happens when these molecules are immersed in water (fully solvated). For each bond, indicate whether the bond becomes weaker, stronger, or stays the same.
(c) Which of these bonds can be broken by just the thermal fluctuations in water with energy of 2.5 kJ/mol?

1



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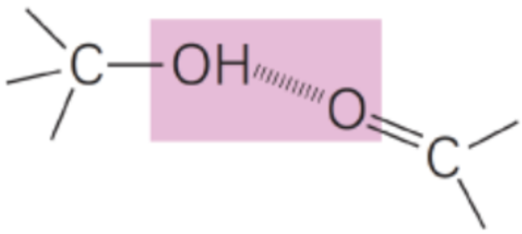

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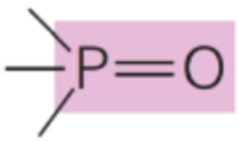

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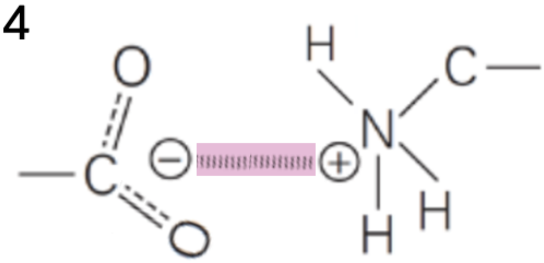


Answers:

a)
1 van der Waals interactions = very weak
2 Hydrogen bonds = weak
3 Covalent bonds = strong
4 Electrostatic interaction = medium

b)
1 van der Waals interactions do not change but the net interactions becomes stronger due to hydrophobic effect

2 Hydrogen bonds become weaker in water
3 Covalent bonds stay the same in water
4 Electrostatic interactions become weaker in water due to shielded charges

c)
In theory, all non-covalent bonds can be broken by thermal fluctuation, but not the covalent bond. The available thermal energy in this case is on average 2.5 kJ/mol with a distribution of values (we will learn about this later). Under these conditions it is most likely to disrupt van der Waals interactions (~0-5 kJ/mol) compared to hydrogen bonds and electrostatic interactions which are more stable (stronger). However, if the hydrogen bonds or electrostatic interactions are assembled under sub-optimal conditions (high distance + poor geometry) their energy could be sufficiently low to be disrupted by thermal fluctuations.

Question 3:

For each statements write whether it is true or false and please explain why:

a) When two atoms come close together, the energy increases due to repulsion between their nuclei.

False: It's the electrons that repel each other since their atomic orbitals start to overlap.

b) Ionic interactions are weaker in nonpolar solvents (such as heptane) as compared to polar solvents (such as water).

False: Nonpolar solvents do not effectively shield charges of the ions, leading to strong attraction. Polar solvents, like water, shield ions and thus reduce the strength of their interaction through dielectric effects.

c) Free atoms can also participate in vdW interactions since they can be polarized by other atoms or groups.

True: Atoms have negative (electron) and positive (proton) charges which makes them polarizable. Therefore, depending on the local atomic environment they can also engage in the vdW.

d) The strength of an N-H•••O=C hydrogen bond is at its maximum when all the atoms are in a straight line.

False: The hydrogen bond N-H•••O is the strongest when the three of these atoms are linear and H is engaging the free electron pair on O. Given the nature of C=O bond, these electron pairs will be located at 120˚ relative to the direction of C=O bond. To give you a visual idea, see hydrogen bonds in DNA shown in the lecture.

e) Under standard lab conditions (atmospheric pressure, room temperature), noble gases such as He, Ne, Ar, Kr, Xe can engage other atoms/molecules via vdW forces but not hydrogen bonds or electrostatic interactions.

True: Similar as the answer to c), they are chemically inert but polarizable. They are not charged and cannot participate in electrostatic interactions. They have free electron pairs but they do not form polar bonds which would make them suitable for hydrogen bonding.

Question 4:

Imagine two functional groups in a protein that are at 3Å from each other interacting via (a) van der Waals, (b) hydrogen bonds or (c) electrostatic interactions. The conformational change in the protein changes their relative orientation to 5Å. Assume that all environmental conditions are the same and the only change was the distance.

What is the relative change in the interaction energy potential (U) induced by this conformational change in case of (a), (b) and (c)? Which interaction type reduces its potential most rapidly.

Answer:

From lecture we know that:

(a) For van der Waals forces $U(r) \sim 1/r^6$

(b) For hydrogen bonds $U(r) \sim 1/r^3$

(c) For electrostatic interactions $U(r) \sim 1/r$

If all other conditions are the same then the ratio of potentials before and after the conformational change would be:

(a) $U_{(3Å)} : U_{(5Å)} = 1/(3Å)^6 : 1/(5Å)^6 = 1/729 : 1/15625 = 21.4$ (fold reduction)

(b) $U_{(3Å)} : U_{(5Å)} = 1/(3Å)^3 : 1/(5Å)^3 = 1/27 : 1/125 = 4.6$ (fold reduction)

(b) $U_{(3Å)} : U_{(5Å)} = 1/(3Å)^1 : 1/(5Å)^1 = 1/3 : 1/5 = 1.7$ (fold reduction)

Van der Waals interaction shows the greatest dependance on distance and reduces its interaction potential (U) most rapidly.

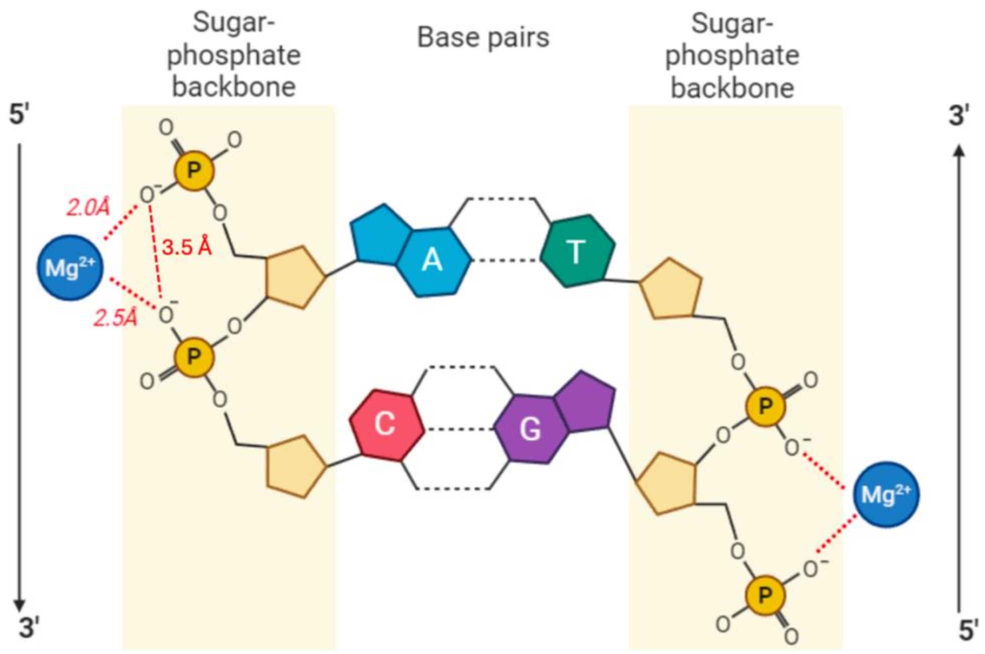
Question 5:

Magnesium ions (Mg^{2+}) play a crucial role in stabilizing DNA structure and are essential cofactors for DNA polymerases during replication. Mg^{2+} binds to the phosphate groups of the DNA backbone to neutralize and stabilize the DNA helix. The positively charged Magnesium is surrounded by two negatively charged phosphate backbones. Assume that all charges lie on the same line. Calculate the electrostatic energy potential (U) of the entire system involving these 3 charged groups in the following two conditions:

a) The interaction takes place in water (D=78.5).

b) The interaction takes place in vacuum (D=1).

Assume the permittivity of the vacuum $\epsilon_0 = 8.854 \times 10^{-12}$ F·m^{-1} (C^2·J^{-1}·m^{-1}) and the unit charge is 1.602×10^{-19} C. To determine the energy potential for one mole of ion combinations (i.e., J/mol) you will need the Avogadro's number 6.02×10^{23} mol^{-1}.



Answer:

a) Use the formula to calculate the energy potential (U) for each individual interaction:

$$U(r) = \frac{1}{4\pi\epsilon_0} \frac{1}{D} \frac{q_1 q_2}{r}$$

The values for constants are provided in text and the charges (q) are:

q $_{(Mg2+)}$ = + 2
q $_{(Phosphate)}$ = -1

The distances can be taken from the image and they are:

Interaction 1 (Mg – Phosphate): 2.0Å = 2.0 * 10^{-10} m
Interaction 2 (Mg – Phosphate): 2.5Å = 2.5 * 10^{-10} m
Interaction 3 (Phosphate – Phosphate): 3.5Å = 3.5 * 10^{-10} m

If you plug in the numbers for each interaction you get:

- Interaction 1 (calculated for single ionic interaction)

$$U_{(1)} = \frac{1}{4\pi\epsilon 0} * \frac{1}{D} * \frac{q1*q2}{r} = \frac{8.99*10^9}{78.5} * \frac{(-1)*1602*10^{-19}*(+2)*1.602*10^{-19}}{2.0*10^{-10}} = \mathbf{-2.94*10^{-20}}\ \text{J}$$

The negative sign indicates attractive energy potential. For 1 mole of particles, we need to multiply this number by Avogadro's number:

$U_{(1,M)}$ = -2.94*10^{-20}J x 6.02 *10^{23} mol^{-1}= **-17.7 kJ/mol**

- Interaction 2 (calculated for single ionic interaction)

$$U_{(2)} = \frac{1}{4\pi\epsilon 0} * \frac{1}{D} * \frac{q1*q2}{r} = \frac{8.99*10^9}{78.5} * \frac{(-1)*1602*10^{-19}*(+2)*1.602*10^{-19}}{2.5*10^{-10}} = \mathbf{-2.35*10^{-20}}\ \text{J}$$

The negative sign indicates attractive energy potential. For 1 mole of particles, we need to multiply this number by Avogadro's number:

$U_{(2,M)}$ = -2.35*10^{-20}J x 6.02 *10^{23} mol^{-1}= **-14.2 kJ/mol**

- Interaction 3 (calculated for single ionic interaction)

$$U_{(3)} = \frac{1}{4\pi\epsilon 0} * \frac{1}{D} * \frac{q1*q2}{r} = \frac{8.99*10^9}{78.5} * \frac{(-1)*1602*10^{-19}*(-1)*1.602*10^{-19}}{3.5*10^{-10}} = \mathbf{+0.84*10^{-20}}\ \text{J}$$

The positive sign indicates repulsive energy potential. For 1 mole of particles, we need to multiply this number by Avogadro's number:

$U_{(3,M)}$ = +0.84*10^{-20}J x 6.02 *10^{23} mol^{-1}= **+5.1 kJ/mol**

So the total energy potential can be calculated as a sum of all individual energy potentials.

For a system consisting of single ions:

$U_{(total)} = U_{(1)} + U_{(2)} + U_{(3)}$ = (-2.94*10^{-20} J) + (-2.35*10^{-20} J) + (+0.84*10^{-20} J)

$U_{(total)}$ = - 4.45 * 10^{-20} J

For one mole of such triple ion systems:

$U_{(total,M)}$ = - 26.8 kJ/mol

b) For this part we can also approach the problem using the same equations as above but replacing the dielectric constant to match the vacuum value (D=1). So, the resulting numbers for one mole of particles are:

$U_{(1,M)}$ = **-1389 kJ/mol**
$U_{(2,M)}$ = **-1115 kJ/mol**
$U_{(3,M)}$ = **+400 kJ/mol**

$$\mathbf{U_{(total,M)} = U_{(1,M)} + U_{(2,M)} + U_{(3,M)} = -2104\ kJ/mol}$$

Due to the nature of the equation, the exact numbers in vacuum are greater by the factor equal to the dielectric constant. Biochemically, this means that the electrostatic interaction in water is 78.5 (D_{water}) times weaker than the same interactions in vacuum.